Attorney Docket No.: 015389-002980US Client Reference No.: 018/183C

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

10/053758 10/053758

In re application of:

Cech et al.

Application No.: To be assigned

Filed: Herewith

For: Novel Telomerase

Examiner:

To Be Assigned

Art Unit:

To Be Assigned

INFORMATION DISCLOSURE

STATEMENT UNDER 37 CFR §1.97 and

§1.98

5/21/02

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. In accordance with 37 CFR §1.98(d), copies of references Q-S can be found in co-pending parent Application No. 09/843,676, filed April 26, 2001 (Attorney Docket no. 015389-002943US). Copies of the other references can be found in parent Application No. 08/854,050, filed May 9, 1997, now U.S. Patent No. 6,261,836 (Attorney Docket No.: 015389-002940US). If the examiner would like additional copies of these references, applicants will happily provide them.

It is respectfully requested that the cited information be expressly considered during the prosecution of this application, and the reference be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

<u>PATENT</u>

Cech et al.

Application No.: To be assigned

Page 2

Applicant believes that no fee is required for submission of this statement, since it is being submitted prior to the first Office Action. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No.

Respectfully submitted,

Reg. No. 47,163

TOWNSEND and TOWNSEND and CREW LLP Two Embarcadero Center, 8<sup>th</sup> Floor San Francisco, California 94111-3834 Tel: 650-326-2400

Fax: 650-326-2422

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Page 1

Sheet

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Substitute for form 1449B/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known					
Application Number	To be assigned				
Filing Date	Herewith Cech, Thomas R.				
First Named Inventor					
Group Art Unit	To Be Assigned				
Examiner Name	To Be Assigned				
Attorney Docket Number	015389-002980US				
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				U.S. PATENT DOCUM	IENTS	
Examiner Initials *	Cite No.'	U.S. Patent Doo Kind ( Number (if kno	Code <sup>2</sup>	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	<del></del>		T	Tanenholtz et al.	06-18-74	
	A	3,817,837	<del> </del>	Schuurs et al.	11-26-74	
	В	3,850,752	<del> </del>	Kronick et al.	02-17-76	
	C	3,939,350	<del> </del>	Ullman et al.	12-01-76	
	D	4,275,149	<del> </del>	Litman et al.	06-23-81	
	E F	4,273,149	<del> </del>	Maggio	07-07-81	
		4,366,241	-	Tom et al.	12-28-82	
	G H	4,683,195	+	Mullis et al.	07-28-87	
	<del>                                     </del>	4,683,202	+	Mullis	07-28-87	
	<del>                                     </del>	4,816,567	+	Cabilly et al.	03-28-89	
	K	4,965,188	+	Mullis et al.	10-23-90	
	<del>                                     </del>	5,489,508		West et al.	02-06-96	
	M	5,583,016		Villeponteau et al.	12-10-96	
	- N	5,747,317		Cao	05-05-98	
	+ ;;	5.770,422	1	Collins	06-23-98	
	P	6.093,809		Cech, et al.	07/25/00	
	1 0	6,258,535	B1	Villeponteau et al.	07-10-01	
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				FOREIG	N PATENT DOCL	JMENTS	Pages, Columns, Lines.	
		For	eign Patent Docu	ument	Name of Patentee	Date of Publication of	Where Relevant	i
Examiner Initials*	Cite No.1	Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)	or Applicant of Cited Document	Cited Document MM-DD-YYYY	Passages or Relevant Figures Appear	T <sup>6</sup>
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	Z	PCT	WO 96/40868			12-19-96		<b></b> _
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	AB	PCT	WO 98/01543			01-15-98		
	AC	PCT	WO 98/07838			03-05-98	<u> </u>	
	AD	PCT	WO 98/08938			02-26-98		

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Herewith Cech, Thomas R. Group Art Unit To Be Assigned To Be Assigned Examiner Name (use as many sheets as necessary) 015389-002980US Attorney Docket Number of Page 2 Sheet

				FOREIG	N PATENT DOCL	JMENTS		
Examiner Initials*	Cite No.1	For Office <sup>3</sup>		nent nd Code <sup>5</sup>	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
	AE	PCT	WO 98/21343			05-22-98		
	AF	PCT	WO 98/23759			06-98		
	AG	PCT	WO 98/37181			08-27-98		
	AH	PCT	WO 98/45450			10-15-98		
	Al	PCT	WO98/59040			12-30-98		
	AJ	PCT	WO99/01560			01-14-99		

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examin er Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T 2
made	AK	1994 Genome Issue of Science (265:1981f)	
	AL	Anderson and Young, "Quantitative Filter Hybridization" in Nucleic Acid Hybridization pp73-111 (1985)	
	AM	Ausubel et al., Current Protocols in Molecular Biology, John Wiley & Sons, New York NY (1989)	
	AN	Autexier et al., "Reconstitution of human telomerase activity and identification of a minimal functional region of the human telomerase RNA," (1996) EMBO J, 15:5928	
	AO	Autexier, C. et al, "Telomerase and cancer: revisiting the telomere hypothesis," Trends in Biochemical Sciences, 10 (21): 387-391 (1996).	
	AP	Auxexier and Greider, "Functional reconstitution of wild-type and mutant <i>Tetrahymena</i> telomerase," (1994) <i>Genes Develop.</i> , 8:563	
	AQ	Avilion, A., "Characterization and expression of human telomerase," Dissertation Abstracts International, 56 (11) 5930-B (1996).	
	AR	Barinaga, M., "The Telomerase Picture Fills In," Science 276:528-529 (1997).	
	AS	Berger and Kimmel, Guide to Molecular Cloning Techniques, Meth. Enzymol., vol. 152, Academic Press, San Diego CA (1987)	

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STATEMENT BY APPLICANT

Page 3 Sheet

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
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Tituais	AT	Biessmann et al., "Addition of Telomere-Associated HeT DNA Sequences "Heals" Broken Chromosome Ends in Drosophila," Cell 61:663 [1990].	
	AU	Bitter et al., "Expression and secretion vectors for yeast," Meth Enzymol., (1987) 153:516	
	AV	Blackburn and Chiou, "Non-nucleosomal packaging of a tandemly repeated DNA sequence at termini of extrachromosomal DNA coding for rRNA in Tetrahymena," (1981) <i>Proc. Natl. Acad. Sci.</i> , 78:2263	
	AW	Blackburn and Gall, " A tandemly repeated sequence at the termini of the extrachromosomal ribosomal RNA genes in <i>Tetrahymena</i> , " (1978) <i>J. Mol. Biol.</i> , 120:33	
	AX	Blackburn, "Telomerases," (1992) Ann. Rev. Biochem., 61:113	
	AY	Bodnar et al., "Extension of Life-Span by Introduction of Telomerase into Normal Human Cells," (1998) Science, 279:349	
	AZ	Bradford, "A Rapid and Sensitive method for the Quantitation of Microgram Quantities of Protein Utilizing the Principle of Protein-Dye Binding," (1976) <i>Anal. Biochem.</i> , 72:248	
	ВА	Braunstein et al., "Transcriptional silencing in yeast is associated with reduced nucleosome acetylation," (1993)  Genes Develop., 7:592	_
	ВВ	Calvio et al., "Identification of hnRNP P2 as TLS/FUS using electrospray mass spectrometry," (1995) RNA, 1:724	
<u> </u>	ВС	Caruthers et al., "New chemical methods for synthesizing polynucleotides," (1980) Nucleic Acids Res. Symp. Ser., 215-223	
	BD	Chan and Tye, "Organization of DNA sequences and replication origins at yeat telomeres, " (1983) Cell, 33:563	
	BE	Colbere-Garapin et al., "A new dominat hybrid selective marker for higher eukaryotic cells," (1981) J. Mol. Biol., 150:1	
	BF	Cole et al., "The EBV-hybridoma technique and its application to human lung cancer," Monoclonal Antibodies and Cancer Therapy, Alan R. Liss Inc., New York NY 77-96 (1985)	
	BG	Collins et al., "Purification of Tetrahymena telomerase and cloning of genes encoding the two peotein components of the enzyme," (1995) Cell, 81:677	
	ВН	Collins, K., "Structure and Function of Telomerase," Curr. Op. Cell. Biol. 8:374-380 (1996).	

	Date
Examiner	Considered
Signature	Considered

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Initials *	BI	Conrad et al., "RAP1 protein interacts with yeast telomers in vivo: Overproduction alters telomere structure and decreases chromosome stability," (1990) Cell, 63:739	
	BJ	Coombs, Dictionary of Biotechnology, Stockton Press, New York NY (1994)	
	вк	Cote et al., "Generation of human monoclonal antibodies reactive with cellular antigens, " (1983) <i>Proc. Natl. Acad. Sci.</i> , 80:2026	
	BL	Counter et al., "The catalytic subunit of yeast telomerase," (1997) Proc. Natl. Acad. Sci., 94:9202	
	ВМ	Creighton, Proteins, Structures and Molecular Principles, WH Freeman and Co, New York NY [1983].	
	BN	Dieffenbach and Dveksler. PCR Primer, a Laboratory Manual, Cold Spring Harbor Press, Plainview NY (1995)	
	во	Duplaa et al., "Quantitative analysis of polymerase chain reaction products using biotinylated dUTP incorporation," (1993) Anal. Biochem., 212:229	_
	BP	Fang et al., "Oxytricha telomere-binding protein: separable DNA-binding and dimerization domains of the $\alpha$ -subunit," Genes Develop. 7:870 (1993) and Gray et al., (1991) Cell 67:807	
	BQ	Feng et al., "The RNA Componant of Human Telomerase," (1995) Science, 269:1236	-
	BR	GenBank Accession No. AA281296	
	BS	Genbank accession no. AA299878	-
	ВТ	Genbank accession no. AA311750	-
	BU	Gilley et al., "Altering specific telomerase RNA template residues affects active site function," (1995) Genes Develop., 9:2214	-
	BV	Gottschling and Cech, "Chromatin Structure of the Molecular Ends of Oxytricha Mononuclear DNA: Phased Nucleosomes and a Telomeric Complex," (1984) Cell, 38:501	-
	BW	Gottschling and Zakian, "Telomere proteins: specific recognition and protection of the natural termini of Oxytricha macronuclear DNA," (1986) Cell 47:195	

Examiner Signature	Date Considered	Little if act in conformance

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		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examin er Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T 2
	вх	Grant et al., Meth Enzymol., (1987) 153:516-544	
	BY	Greenwood et al., "Phylogenetic relationships within the class oligohymenophorea, phylum ciliophora, inferred from the complete small subunit rRNA gene sequences of Colpidium campylum, Glaucoma chattoni, and Opisthonecta henneguyi," (1991) J. Mol. Evol., 3:163	
	BZ	Greider and Blackburn, "A telomeric sequence in the RNA of Tetrahymena telomerase required for telomere repeat synthesis," (1989) Nature, 337:331	
	CA	Greider and Blackburn, "Identification of a specific telomere terminal transferase activity in Tetrahymena extracts," (1985) Cell. 43:405	
	СВ	Greider, "Telomerase is processive," (1991) Mol. Cell. Biol., 11:4572	
	СС	Greider, "Telomere Length Regulation," (1996) Ann. Rev. Biochem., 65:337	-
	CD	Hampton et al., Serological Methods a Laboratory Manual, APS Press, St Paul MN (1990)	-
	CE	Harrington et al., "A Mammalian Telomerase-Associated Protein," (1997) Science, 275:973	
	CF	Harrington et al., "Human telomerase contains evolutionarily conserved catalytic and structural subunits," (1997) Genes Dev., 11:3109	
	CG	Hartman and Mulligan, "Two dominant-acting selectable markers for gene transfer studies in mammalian cells," (1988) Proc. Natl. Acad. Sci., 85:8047	
	СН	Henderson and Blackburn, "An overhanging 3' terminus is a conserved feature of telomeres," (1989) <i>Mol Cell. Biol.</i> , 9:345	-
	CI	Hillier, et al., Direct Submission to GenBank, EST Database, Accession No. W70315, Available Oct. 17, 1996.	
	CJ	Horn et al., "Synthesis of oligonucleotides on cellulose. Part II: design and synthetic strategy to the synthesis of 22 oligodeoxynucleotides coding for gastric inhibitory polypeptide (GIP)," (1980) Nucleic Acids Res. Symp. Ser., 225-232	-
	СК	Hudson et al., "An STS-based map of the human genome," (1995) Science, 270:1945	
	CL	Huse et al., "Generation of a large combinatorial library of the immunoglobulin repertoire in phage lambda," (1989) Science, 246:1275	

Examiner Signature	Date Considered	
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		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examin er initials *	Cite	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T 2
Tituais	СМ	Kilian et al., "Isolation of a candidate human telomerase catalytic subunit gene, which reveals complex splicing patterns in different cell types," (1997) Hum. Mol. Genet., 6:2011	
	CN	kipling and Cooke, "Hypervariable ultra-long telomeres in mice," (1990) Nature 347:400	
	со	klobutcher et al., "All gene-sized DNA molecules in four species of hypotrichs have the same terminal sequence and an unusual 3' terminus," (1981) Proc. Natl. Acad. Sci., 78:3015	
	СР	Koehler and Milstein, "Continuous cultures of fused cells secreting antibody of predefined specificity," (1975) Nature 256:495	
	ca	Kosbor et al., "The production of monoclonal antibodies from human lymphocytes," (1983) Immunol. Today 4:72	
	CR	Lamond and Sproat, (1994)"Isolation and Characterization of Ribonucleoprotein Complexes," pp103-140	
	cs	Lamond et al., "Probing the structure and function of U2 snRNP with antisense oligonucleotides made of 2'-OMe RNA," (1989) Cell, 58:383	
	СТ	Lendvay et al., "Senescence mutants of Saccharomyces cerevisiae with a defect in telomere replication identify three additional EST genes," (1996) Genetics, 144	
	CU	Lingler et al., "Purification of telomerase from Euplotes adeiculatus: requirement of a primer 3' overhang," (1996) Proc. Natl. Acad. Sci., 93:10712	
	cv	Lingler et al., "Reverse transcriptase motifs in the catalytic subunit of telomerase," (1997) Science, 276:561	
	cw	Lingner et al., "Telomerase RNAs of different ciliates have a common secondary structure and a permuted template, " (1994) Genes Develop., 8:1984	
	СХ	Lingner et al., "Telomerase and DNA End Replication: No Longer a Lagging Strand Problem?," (1995) Science 269:1533	
	CY	Lowy et al., "Isolation of transforming DNA: Cloning the hamster aprt gene," (1980) Cell, 22:817	
	cz	Lundblad, V. et al., "RNA-dependent polymerase motifs in EST1: tentative identification of a protein component of an essential yeast telomerase," Cell, 60 (5):29-30 (1990).	
	DA	Lustig and Petes, Identification of yeast mutants with altered telomere structure," (1986) <i>Proc. Natl. Acad. Sci.</i> , 83:1398	

Examiner Date
Signature Considered

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muso	DB	Lustig, A., "The Identification of Telomerase Subunits: Catalysing Telomere Research," Trends Cell. Biol. 7.299-302 (1997).	
	DC	Maddox et al., "Elevated serum levels in human pregnancy of a molecule immunochemically similar to eosinophil granule major basic protein," (1983) J. Exp. Med., 158:1211	
	DD	Makarov et al., "Nucleosomal Organization of Telomere-Specific Chromatin in Rat," (1993) Cell, 73:775	
	DE	McEachern and Blackburn, "runaway telomere elongation caused by telomerase RNA gene mutation," (1995)  Nature, 376:403	
	DF	Melby et al., "Quantitative measurement of human cytokine gene expression by polymerase chain reaction," (1993) J. Immunol. Meth., 159:235	
	DG	Merrifield, "Solid phase peptide synthesis. I. The synthesis of a tetrapeptide," (1963) J. Am. Chem. Soc., 85:2149	
	DH	Meyerson et al., "hEST2, the Putative Human Telomerase Catalytic Subunit Gene, Is Up-Regulated in Tumor Cells and during Immortalization," (1997) Cell, 90:785	
	DI	Murray, In McGraw Hill Yearbook of Science and Technology, (1992) McGraw Hill, New York NY, pp 191-196	
	DJ	Nakamura et al., "Telomerase Catalytic Subunit Homologs from Fission Yeast and Human," (1997) Science, 277:955	
	DK	Nakayama et al., "Cloning of a Candidate cDNA Encoding a Proteinaceous Component of Mammalian Telomerase," Mol. Biol. Cell. Abstracts Supp. 7 p. 286a, .sctn. 1664 (1996).	
	DL	Nakayama et al., "TLP1: A Gene Encoding a Protein Component of Mammalian Telomerase Is a Novel Member of WD Repeats Family." (1997) Cell,88:875	
	DM	Nielsen et al., (1993) "Peptide nucleic acids (PNAs): Potential antisense and anti-gene agents," Anticancer Drug Des., 8:53	
	DN	Oka et al., "Inverted terminal repeat sequence in the macronuclear DNA of Stylonychia pustulata, " (1980) Gene, 10:301	
	DO	Olovnikov, "A theory of marginotomy: The incomplete copying of template margin in enzymic synthesis of polynucleotides and biological significance of the phenomenon," (1973) <i>J. Theor. Biol.</i> , 41:181	
	DP	Orlandi et al., "Cloning immunoglobulin variable domains for expression by the polymerase chain reaction," (1989) Proc. Natl. Acad. Sci., 86:3833	

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	DQ	Prescott, "The DNA of ciliated protozoa," (1994) Microbiol. Rev., 58:233	
	DR	Price, (1993) Blood Rev., 7:127	
	DS	Rhodes et al., "Transformation of maize by electroporation of embryos," (1995) Meth. Mol. Biol., 55:121	
	DT	Roberge et al., "A strategy for a convergent synthesis of N-linked glycopeptides on a solid support," (1995) Science, 269:202	
	DU	Romero and Blackburn, "A conserved secondary structure for telomerase RNA, " (1991) Cell, 67:343	
	DV	Sambrook et al., Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview NY (1989)	
	DW	Sandell et al., "Transcription of yeast telomere alleviates telomere position effect without affecting chromosome stability, "(1994) Proc. Natl. Acad. Sci., 91:12061	
	DX	Sanger et al., "DNA sequencing with chain-terminating inhibitors," Proc. Natl. Acad. Sci., 74:5463 [1977].	
	DY	Scharf et al., "Heat stress promoters and transcription factors," (1994) Result Probl. Cell Differ. 20:125	
	DZ	Shampay and Blackburn, "Generation of telomere-length heterogeneity in Saccharomyces cerevisiae," (1988) Proc. Natl. Acad. Sci., 85:534	
	EA	Sheen and Levis, "Transposition of the LINE-like retrotransposon TART to <i>Drosophila</i> chromosome termini," (1994) <i>Proc. Natl. Acad. Sci.</i> , 91:12510	
	EB	Singer and Gottschling, "TLC1: Template RNA Component of Saccharomyces cerevisiae Telomerase," (1994) Science 266:404	
	EC	Singer, M., "Unusual Reverse Transcriptases," J. Biol. Chem. 270(42):24623-24626 (1995).	
	ED	Starling et al., "Extensive telomere repeat arrays in mouse are hypervariable," (1990) Nucleic Acids Res., 18:6881	
	EE	Swanton et al., "Arrangement of Coding and Non-coding Sequences in the DNA Molecules Coding for rRNAs in Oxytricha sp" (1980) Chromosoma 77:203	

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1111000	EF	Tommerup et al., "Unusual chromatin in human telomeres," (1994) Mol. Cell. Biol., 14:5777	
	EG	Trask, "Fluorescence in situ hybridization: application in cytogenetics and gene mapping," (1991) <i>Trends Genet.</i> , 7:149	
	EH	Verma et al., "Human Chromosomes: A Manual of Basic Techniques," Pergamon Press, New York NY (1988)	
	EI	Watson, "Origin of concatermeric T7 DNA, " (1972) Nature New Biol., 239:197	
	EJ	Weinrich et al., "Reconstitution of human telomerase with the template RNA component hTR and the catalytic protein subunit hTRT," (1997) Nat. Genet., 17(4):498	
	EK	Wellinger et al., "Origin activation and formation of single-strand TG <sub>1-3</sub> tails occur sequentially in late S phase on a Yeast linear plasmid," (1993) <i>Mol. Cell. Biol.</i> , 13:4057	
	EL	Wellinger et al., "Saccharomyces Telomeres Acquire Single-Strand TG <sub>1-3</sub> Tails Late in S Phase," (1993) Cell 72:51	
	EM	Whitehead Institute/MIT Center for Genome Research, Genetic Map of the Mouse, Database Release 10, APril 28, 1995	 
	EN	Wigler et al., "Transfer of purified herpes virus thymidine kinase gene to cultured mouse cells," (1977) Cell, 11:223	
	EO	Wigler et al., "Transformation of mammalian cells with an amplifiable dominant-acting gene," (1980) Proc. Natl. Acad. Sci., 77:3567	_
	EP	Winter and Milstein, "Man-made antibodies," (1991) Nature, 349:293	<u> </u>
	EQ	Wright et al., "Saccharomyces telomeres assume a non-nucleosomal chromatin structure, " (1992) Genes Develop., 6:197	
	ER	Yu et al., "In vivo alteration of telomere sequences and senescence caused by mutated Tetrahymena telomerase RNAs," (1990) Nature, 344:126	-
	ES	Zahler and Prescott, "Telomere terminal transferase activity in the hypotrichous ciliate Oxytricha nova and a model for replication of the ends of linear DNA molecules," (1988) Nucleic Acids Res., 16:6953	$\perp$
-	ET	Zakian, Telomeres: Beginning to Understand the End," (1995) Science 270:1601	

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Application Number	To be assigned	
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First Named Inventor	Cech, Thomas R.	
Group Art Unit	To Be Assigned	
Examiner Name	To Be Assigned	
Attorney Docket Number	015389-002980US	

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muoio	EU	Zaug et al., "Catalysis of RNA Cleavage by a Ribozyme Derived from the Group I Intron of Anabaena Pre-tRNA Leu,"	
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